DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-408

Bertek Pharmaceuticals, Inc.
Attn: Charity M. Schuller, Pharm.D.
Senior Associate, Regulatory Affairs
P.O. Box 14149
Research Triangle Park, NC 27709-4149

Dear Dr. Schuller,

Please refer to your new drug application (NDA) dated December 14, 2001, received December 17, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for MENTAX®–TC (butenafine HCl) Cream, 1%.

We acknowledge receipt of your submissions dated December 20 and 31, 2001; January 11 and 31, February 20 and 27, March 21, April 10, 12 and 18, May 9, June 3, 11 and 18, July 12, August 5 and 30, September 5, 6, 9, 23 and 26, October 7, 11 and 15, 2002.

This new drug application provides for the use of MENTAX®–TC (butenafine HCl) Cream, 1%, for the topical treatment of tinea (pityriasis) versicolor due to *Malassezia furfur* (formerly *Pityrosporum orbiculare*).

We completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert, immediate container and carton labels). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, please designate this submission "**FPL for approved NDA 21-408.**" Approval of this submission by FDA is not required before the labeling is used.

We remind you of your postmarketing study commitment in your submission dated October 15, 2002. This commitment is listed below.

A Phase 4 study should be conducted to address the concern of whether the drug product can alter the production of UV-induced skin tumors. To satisfy this need, you may propose and conduct either a photocarcinogenicity study in hairless mice or a short-term study that evaluates markers of UV-induced skin damage. Either animal or human models may be acceptable.

Markers of UV induced damage that may be appropriate endpoints could include, but are not limited to, MED, thymine dimers or p53 levels. A protocol should be submitted to the relevant IND for review and concurrence prior to study initiation.

This recommendation is consistent with Division and CDER practice for a topical drug product used on sun exposed skin for a chronic intermittent indication. Please refer to the Pharmacology/ Toxicology draft guidance on Photosafety Testing on the CDER website (http://www.fda.gov/cder/guidance/index.htm).

Commitment Category:	NON-CLINICAL TOXICOLOGY	
	Protocol Submission:	Within 4 months of the date of this letter
	Study Start:	Within 6 months of the date of the approval of the protocol
	Final Report Submission:	Within 12 months after the study completion.

Protocols, data, and final study reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "Postmarketing Study Protocol", "Postmarketing Study Final Report", or "Postmarketing Study Correspondence."

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens must contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (21 CFR 314.55).

Based on the information submitted, we conclude the following:

For the topical treatment of tinea (pityriasis) versicolor due to Malassezia furfur (formerly Pityrosporum orbiculare),

- We are waiving the pediatric study requirement for this action for this application for pediatric patients below the age of 12 years since tinea versicolor is uncommon in pediatric patients below 12 years of age.

- You have fulfilled the pediatric study requirement at this time for pediatric patients 12 years of age and older.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert(s) directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, please call Frank H. Cross, Jr., M.A., CDR, Senior Regulatory Management Officer, at (301) 827-2020.

Sincerely,

{See appended electronic signature page}

Jonathan K. Wilkin, M.D.
Director
Division of Dermatologic & Dental Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Jonathan Wilkin

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